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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In the Application of:

NARENDRA S. YADAV

CASE NO.: CL1127 US CIP 1

APPLICATION NO.: 09/715294

GROUP ART UNIT: 1638

FILED: NOVEMBER 17, 2000

EXAMINER: MEHTA, A

FOR: HERITABLE VIRAL EXPRESSION SYSTEM IN PLANTS

**DECLARATION OF JOAN T. ODELL UNDER 37 CFR 1.132**

Assistant Commissioner for Patents
Washington, D.C. 20231

This Declaration is submitted in partial response to the Office Action mailed on 17 February 2004.

I, Joan Tellefsen Odell, declare as follows:

1. I am a citizen of the United States of America, residing at P.O. BOX 826, Unionville, Pennzylvania 19375.

2. I received a Bachelor of Arts degree in Biology from the University of California, San Diego in 1975. I received a Doctor of Philosophy in 1981 from the University of California, San Diego, in Molecular Biology. I held a Postdoctoral Fellowship in Molecular Biology at Rockefeller University from 1981 to 1985.

3. From 1985 to 1987 I was employed as a Principal Investigator by E.I. du Pont de Nemours and Company, Wilmington, DE, in the Biology group of the Company's Central Research and Development organization. From 1987 to 2001 I held the title of Principal Investigator in the Agricultural Biotechnology organization, later called Crop Genetics, in the same company. This group addressed genetic engineering of plants for crop improvement. My particular area is in the regulation of gene expression in plants. I am an inventor on 11 US issued patents and 11 pending published US patent applications

as a result of my work in DuPont; additionally, I am a principle or co-author of over 13 technical publications since 1987 and a review chapter. I have presented several invited lectures in the United States and internationally since 1987. I have reviewed grant applications for several organizations including the USDA and NIH. I have reviewed manuscripts for several different scientific journals including Plant Molecular Biology.

From 2001 to 2003 I was a Six Sigma Black Belt in the Central Research and Development Department and currently, I hold the position of Patent Liaison in the Patent group of the E.I. du Pont de Nemours and Company's Central Research and Development organization.

4. As a result of my education and experience, I believe that I am an expert in plant gene expression and certainly capable of testifying about the understanding of those skilled in the art relating to attempts to develop a conditional transgene expression and trait removal system in plants based on site-specific recombination. Specifically, I believe that I may provide insight about the state of the art over the last 15 years, and particularly as of November 2000, which is when I understand that Dr. Narendra Yadav filed in the United States a patent application (US 09/715294) relating to the use of a dual site specific recombination system for conditional transgene expression and trait removal in plants. I have reviewed the correspondence in this application including the pending Non-Final Office Action, mailed 17 February 2004, which contains a rejection of Claims 39-41, 43, 70, 80, 81, 83, and 85 under 35 U.S.C. 103(a).

5. Among my publications, I am a co-author of the articles "Site-directed recombination in the genome of transgenic tobacco" published in *Molecular & General Genetics* (volume 223(3), pp 369-78, Sept 1990) and "Use of Site-Specific Recombination Systems in Plants" (pp 219-270) in Homologous Recombination and Gene Silencing in Plants, edited by J. Paszkowski (Kluwer Academic: Dordrecht, Germany (July, 1994)). My understanding is that in the examination of Dr. Yadav's US patent application relating to the use of a dual site specific recombination system for conditional transgene expression and trait removal in plants, the United States Patent and Trademark Office has taken the position that my articles:

- Teach the use of the Cre/lox recombination system in transgenic tobacco and propose that turning on expression of a marker gene by controlling Cre expression in a regulated manner would provide the ability to follow cell lineages in the plant.
- Teach uses of various site-specific recombination systems in plants and assert that the versatility and high recombination frequency of these systems allow their use as tools for a wide range of studies and applications and that the systems can be used to control gene expression in any plant generation and/or tissue.

6. It is also my understanding that in the examination of Dr. Yadav's US patent application relating to the use of a dual site specific recombination system for

conditional transgene expression and trait removal in plants, the United States Patent and Trademark Office has taken the position that the article published by Lloyd et al. titled "Functional expression of the yeast FLP/FRT site-specific recombination system in *Nicotiana tabacum*" and published in *Molecular & General Genetics* (volume 242(6), pp 653-7, March 1994) teach the use of the FLP/FRT site-specific recombination system in stably transformed tobacco plants.

7. Furthermore, it is my understanding that in the examination of Dr. Yadav's US patent application relating to the use of a dual site specific recombination system for conditional transgene expression and trait removal in plants, the United States Patent and Trademark Office has taken the position that it would have been obvious to one skilled in the art to combine:

a.) the teachings from my publications cited above;
b.) the teachings from Lloyd et al.; and
c.) the general knowledge of one of skilled in the art in November 2000 concerning specific promoters and transgenes;

to derive the invention disclosed in Dr. Yadav's US patent application.

8. Based on my academic training and professional experience, I believe that at the time my articles were written and published in 1990 and 1994, the person of skill in the art would not have had a reasonable expectation of success for combining multiple site specific recombinaase systems together in one gene regulation scheme in a single plant for regulated or conditional gene expression because:

The statement in Odell and Russell (1994, Use of Site-Specific Recombination Systems in Plants, Homologous Recombination and Gene Silencing in Plants, Paszkowski, ed. P219-170) that the effectiveness of the recombinase in *Nicotiana tobacum* "is quite impressive" must be put in context with the entire paragraph. As stated also on p260, the site-specific recombination systems "all have bacteriophage genomes or plasmids as their natural substrates". Thus at that time it was thought that the recombinases would be able to function <u>not at all or rarely</u> on a substrate that is as complex as a chromosome in a plant cell. The words "quite impressive" refer to effectiveness relative to expectations of <u>no or barely detectable</u> recombination. The use of systems involving activation of selection markers to detect recombinase activity in both Odell et al. (1990, MGG 223:369-378) and Lloyd and Davis (1994, MGG 242:6530657) shows that the expectation that successful recombination would occur was low; the selection was expected to be necessary for identifying any cells in which recombination occurred.

Thus at the time of these references, no idea that two different SSR systems could effectively regulate gene expression in a complex combined system was being

proposed. This type of system requires that the activities of two different recombination systems be efficiently coordinated in the same cell, not just in the same plant.

9. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the subject application or of any patent issuing thereon.

Joan Tellefsen Odell

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DATE: Aug. 10, 2004